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A Primary Orbital Myxoid Liposarcoma

Clinical History and Investigation

An 81 year-old caucasian male patient presented to ophthalmologist with double vision one week after left phacoemulsification with intraocular lens implantation under local anaesthetics. On examination, visual acuity is 6/9 LE and 6/7.5 RE. There is noticeable left non-axial proptosis. The only significant ophthalmic history is bilateral pseudophakia. However, he had fairly extensive medical history including hypertension, ischaemic heart disease, atrial fibrillation, congestive heart failure, previous angioplasty and normocytic anaemia. MRI scan showed a homogenous enhancement of left medial wall with an extraconal orbital mass measuring 42x22x27 mm. This mass caused minimal displacement of left optic nerve laterally with moderate displacement of the left superior rectus and medial rectus muscles. The mass did not extend into the left nasal cavity or paranasal sinuses. There was no haemorrhage or intracranial enhancement. The working diagnosis was – suspicious of lymphoma.

An incisional biopsy of the orbital mass was performed. The specimen was a firm white nodule of up to 10 mm in maximum dimension. Microscopy showed a fragment of a malignant neoplasm, composed of sheets of tumour cells with short spindly to oval-shaped nuclei and indistinct cell borders, set in a slightly myxoid matrix. Most of the tumour cells show a signet ring lipoblast morphology and occasional multivacuolated forms are also present. There is mild to moderate nuclear pleomorphism and scattered mitotic figures are seen. On immunohistochemistry, these tumour cells are negative for S100 and CD34. FISH (Fluorescent In-situ Hybridization) analysis using the Vysis DDIT3 break-apart probe showed the presence of break-apart signals in the tumour cells in keeping with a DDIT3 translocation. There is no evidence of MDM2 gene amplification on FISH analysis. A diagnosis of myxoid liposarcoma was made.

In view of his extensive co-morbidities, instead of primary orbital exenteration, the multidisciplinary team concluded that a radical pre-operative neo-adjuvant radiotherapy (XRT) would be more appropriate treatment at the time. Following the XRT, the visual acuity of left eye deteriorated to 1/36. MRI scan showed an excellent response to the XRT with tumour only restricted to the orbit. CT CAP showed no evidence of metastasis. At this point, the patient was fit enough to undergo a lid-sparing left orbital exenteration.

Histological examination of the orbital exenteration specimen showed a low grade / Trojani grade 1 myxoid liposarcoma occupying the supero-medial quadrant of the orbital soft tissue with intraconal extension, demonstrating partial response to pre-operative XRT. The tumour extends to the supero-medial margin but not involving the left globe. It was staged as ypT3 Nx Mx.

He was followed up regularly for 5 years. Despite not receiving adjuvant XRT or chemotherapy (CRT), he did not show clinical or radiological evidence of local recurrence or metastasis. Unfortunately, he died in his sleep following general health decline 6 years post-diagnosis.

Discussion

Liposarcoma is subclassified into four subtypes: Well differentiated liposarcoma (WDLPS)/ Atypical lipomatous tumour (depending on location), Dedifferentiated liposarcoma (DDLPS), Myxoid liposarcoma (MLPS) and Pleomorphic liposarcoma (PLPS)(1). Primary orbital liposarcoma is a rare malignancy with less than 100 reported cases in the literature (2). As such, consensus and development of its management remains challenging. In a recent retrospective review of liposarcoma of nearly 17000 patients, only 0.12% (n=19) involves the orbit. Of these, MLPS constitutes the commonest subtype (31.6%, n=6), followed by WDLPS (26.3%, n=5) (3).

Unlike other subtypes of liposarcoma which typically demonstrate amplification of MDM2 gene, Myxoid liposarcoma is distinguished by recurrent translocations, mainly t(12;16) (q13;p11.2) which result in fusion of FUS with DDIT3. Rarely (2-5%), t(12;22) (q13;q12) translocation is present, resulting in fusion of EWSR1 with DDIT3 (4).

Studies have identified the WDLPS subtype as having the most favourable prognosis. This subtype exhibits locally aggressive behaviour without the tendency to metastasise, unless it undergoes dedifferentiation (3, 5, 6). Dedifferentiation occurs in approximately 5% to 15% of cases, with an average onset of 7 to 8 years following diagnosis, although it can occur as late as 16 to 20 years post-diagnosis (3, 7).

Traditionally, due to high rate of local recurrence and relative resistance to radiotherapy (XRT) and chemotherapy (CRT), primary surgical resection remains the mainstay of treatment followed by adjuvant XRT/CRT (8, 9).Vast majority of patients in many case reports and all 6 patients from the series by Madge et al. ended up with orbital exenteration due to local recurrence (5). However, a recent single institute review of 13 patients in China, Gao et al. reported favourable outcome in 10 out of 13 patients who underwent primary surgical resection without exenteration followed by adjuvant XRT, avoiding a significant disfigurement (10).

The role of adjuvant XRT and CRT remains unclear. Our patient had a pre-operative neoadjuvant XRT followed by an orbital exenteration with no evidence of recurrence until his death 6 years post-diagnosis, despite a positive surgical resection margin. Our case also demonstrates the benefit of neo-adjuvant XRT prior to surgical resection. This is particularly helpful in patients who might not be suitable for primary surgery at the time of diagnosis.

Recent advancement in molecular genetics offers several therapeutic targets for liposarcoma. For example, CDK4 is amplified in 90% of WDLPS and DDLPS subtypes, CDK4/6 inhibitors have shown improved progression-free survival in clinical trials (11). In addition, a vaccine targeting the increased NY-ESO-1 expression in MLPS is currently under investigation (12).

Although primary orbital liposarcoma is extremely rare, it is important to include this diagnosis within the differential diagnoses in a patient with orbital mass to avoid misdiagnosis that may lead to inadequate clinical management that could affect the patient's prognosis.

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